

July 25, 2002

Mr. Neal Netzel
Product Specialist
Velsicol Chemical Corporation
10400 West Higgins Road
Suite 600
Rosemont, Illinois 60018

Dear Mr. Netzel:

The Office of Pollution and Toxics is transmitting EPA's comments on the robust summaries and test plan for isodecyl benzoate, posted on the ChemRTK HPV Challenge Program Web site on December 19, 2001. I commend Velsicol Chemical Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Velsicol Chemical Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

**EPA Comments on Chemical RTK Challenge Submission:
Isodecyl Benzoate**

SUMMARY OF EPA COMMENTS

The Sponsor, Velsicol Chemical Corporation, submitted a test plan and robust summaries to EPA on November 21, 2001, for isodecyl benzoate (CAS No. 131298-44-7). EPA posted the submission on the ChemRTK HPV Challenge Web site on December 19, 2001.

EPA has reviewed this submission and has the following conclusions:

1. Physicochemical and Environmental Fate Data. The submitter needs to provide an explanation for two biodegradation tests with conflicting results and characterize the material tested as to the distribution of molecular weights and alkyl branching. The submitter also needs to provide water solubility data at the environmental pH of 7.0.
2. Health Endpoints. EPA disagrees with the submitter that the reproductive toxicity endpoint has been adequately addressed. A reproductive toxicity screening study (OECD TG 421) is necessary to address this endpoint.
3. Ecotoxicity. The submitter proposed no additional toxicity testing. EPA's tentative judgement is that no additional test data are needed to satisfy the needs of the HPV Challenge Program pending receipt of adequate robust summaries and additional information on the chronic invertebrate (reproductive) study.

EPA requests that the submitter advise the Agency within 60 days of any modification to its submission.

EPA COMMENTS ON THE ISODECYL BENZOATE CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The water solubility test was conducted in a pH range of 4.38 to 5.98 instead of the required environmental pH of 7.0. The submitter needs to conduct a water solubility test using a hardness of <180 mg/L CaCO₃ and a pH of 7.0 to mimic environmental test conditions and help explain the ecological test results.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

With the exception that the biodegradation data need to be clarified as detailed below, the test plan for these endpoints is adequate for the purposes of the HPV Challenge Program.

Biodegradation. Results from two tests are substantially different. The submitter needs to explain the conflicting results. The submitter also needs to characterize the material tested as to the distribution of molecular weights and alkyl chain branching. Differences in composition between the test substances might account for the divergent results.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

EPA agrees with the submitter that adequate data are available and no additional testing is necessary for the acute, repeated-dose, genetic, and developmental toxicity endpoints for the purposes of the HPV Challenge Program.

Reproductive Toxicity. The submitter concluded that the reproductive toxicity endpoint is addressed by evaluation of reproductive organs in the 28-day repeated-dose toxicity study and the availability of a developmental toxicity study. EPA disagrees with this conclusion because EPA's guidance specifically states that when effects on reproductive organs have been sufficiently documented in an existing *90-day repeated-dose* study and a developmental toxicity study is available, the reproductive toxicity endpoint can be considered as addressed for the purposes of HPV Challenge Program. The 28-day study is not of a sufficiently long duration for assessing effects on the reproductive organs. Therefore, a reproductive toxicity screening study (OECD TG 421) is necessary to address this endpoint.

Ecotoxicity (fish, invertebrates, algae).

The submitted invertebrate chronic robust summary failed to provide an LOEC at the chemical's aqueous water solubility limit. Adding to this problem is that the submitted water solubility test was not done at pH 7.0. Because the chemical's measured log Kow value is 4.2, and analogous chemicals have shown chronic effects, EPA believes that the chemical may exhibit chronic aquatic toxicity at the true aqueous water solubility limit. Thus, the submitter needs to provide relevant water solubility data to conclude if indeed the chemical was tested at the aqueous water solubility limit in the daphnia chronic study. For this reason, EPA recommends conducting a water solubility test under environmental conditions including a pH of 7 and a hardness of #180 mg/L as CaCO₃. EPA recommends redoing the chronic invertebrate study if the chemical was not tested at the aqueous water solubility limit. Because this chemical is difficult to test due to its low water solubility, guidance on how to test chemicals according to the OECD Guidance Document on Aquatic toxicity Testing of Difficult Substances and Mixtures is available at <http://www.oecd.org/ehs/test/monos.htm>.

The submitter supplied a fish chronic study. This fish study has similar problems as the submitted daphnia chronic study.

SPECIFIC COMMENTS ON THE ROBUST SUMMARIES

Health Effects Statistical methods should be identified in the robust summaries for acute inhalation, repeated dose, developmental, and genetic toxicity.

Acute toxicity. The robust summary for acute inhalation toxicity did not include the frequency of clinical observations, necropsy findings (if performed), or relationships between sub-lethal clinical signs and exposure concentration.

Repeated-dose toxicity. The robust summary did not indicate the number of rats per dose level that displayed signs of toxicity or whether observed behavioral effects were reversible.

Developmental toxicity. The robust summary did not indicate the frequency of clinical observations or incidences of developmental effects.

Ecotoxicity Studies

Fish. Missing acute study details include pH, water hardness, temperature, DO, solvent used, and if the chemical test concentration was measured.

Invertebrates. Missing details include pH, hardness, temperature, DO, and type of solvent and concentration.

Algae. Missing details include pH, hardness, temperature, type and concentration of solvent if used, and temperature.

Invertebrate Chronic. Missing study details include an indication if a solvent was used and concentration, DO, pH, and water hardness. There appears to be a discrepancy in the method and remarks sections for lowest concentrations tested and what is stated in the results section.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modification to its submission.